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Discussion

Dr Shaf Keshavjee *(Toronto, Ontario, Canada).* Dr Ailawadi, that was a very nice presentation. I would like to congratulate your group on demonstrating significant improvements in the outcome of LTX in your center.

Although you have very eloquently explained why you use the old term ''reperfusion injury'' and the OI for comparison of your era outcomes, I think it is very important for the audience to recognize that we need to move toward standardizing nomenclature and measurement parameters for comparison if we are going to make meaningful observations in our patients.

I was quite pleased to see in your presentation the reference to the PGD grading system in your current-era patients. The ISHLT Working Group defined PGD to refer not only to RI but to acknowledge the fact that much of the syndrome of PGD that you see is related to donor factors, such as brain death, infection, aspiration, trauma, and so on, plus ischemia, reperfusion, and the immunologic factors in the recipient, and therefore that findings that you see related to improvement of this syndrome after transplantation might be attributed to many of the factors across the board. I particularly liked your comment about program maturation because it does speak to the attributable factor of increasing improvement in outcomes within the multidisciplinary teams that take care of these patients with increased volumes and increased experience. I do think that recipient factors do play a role in what you have seen because if you look at your data, the table does show that you have a net increase in lower-risk patients, patients with COPD and cystic fibrosis, and a net decrease in the higher-risk patients, patients with pulmonary hypertension and the idiopathic pulmonary fibrosis, and this certainly could contribute to outcomes, although you might have found that in your small sample size.

Therefore my questions are as follows. Do you know when your OPO instituted routine administration of steroids to the donors? This might be a factor in decreasing PGD.

Dr Ailawadi. I do not have the data back in the 1990s when that was initiated. I do know that it has been the routine in the current era.

Dr Keshavjee. That, again, was a transition that happened in the late 1990s in most organ procurement organizations (OPO), so that indeed could have been a factor.

Your study period spans from 1990 to 2006. You chose to split the eras at March 2000. Why did you choose that date? Second, your lung preservation solution, as you mentioned, went from Euro–Collins to University of Wisconsin solution to Perfadex. Did you look at your data separating Perfadex from the high-potassium solutions, and did you find anything interesting there?

Dr Ailawadi. That is a very good question. We chose March 2000 because that is when we analyzed our previous data and our last report had come out. That is when we first recognized that early initiation of ECMO might be beneficial. That might be an arbitrary date, but it is sort of when we made that last conclusion and realized that there might be a difference and became the transition point for this study. We did not analyze by preservation solution. Again, the transition point from Euro–Collins or University of Wisconsin solution started in 1999, and by 2000, we were exclusively using Perfadex, and that was almost superimposed with the March 2000 transition date. We can go back and look at how preservation solution related to RI.

Dr Keshavjee. I think for the purpose of the convenience of analyzing the database, it was probably easier, but it might be more meaningful to go back and look at that to see what role it played in your center.

In terms of the ECMO bridge to recovery, your mortality decreased from 80% to 25%, although the time to institution of

ECMO really did not change. To what do you attribute this improved outcome? Do you think that you are seeing a different form or more quickly recoverable form of PGD, or are there factors in your intensive care unit personnel that might have contributed to this improvement?

Dr Ailawadi. I think there are multiple potential explanations that are very difficult in this small sample size to really understand. I think that the way we handle the ventilator is much different now than it was in the 1990s based on the Acute Respiratory Distress Syndrome Network data. I think there is certainly a heightened awareness of RI or PGD in our intensive care unit, and they might not have been as aware in the early 1990s. I do think the severity of the injury to the lung is likely less severe now than it was in the 1990s. Even though we do not see that based on our incidence, I think the actual amount of injury to the lung has decreased, and we did try to show that when we analyzed the subgroup of patients that had RI, their OI was less.

Dr Keshavjee. You demonstrated a significant increase in PGD in the patients undergoing bilateral LTX. Do you think that this is real, or is it just that you are more able to diagnose PGD in the bilateral patients, whereas patients undergoing single LTX have the advantage of having the residual native lung to provide some function in some cases.

Dr Ailawadi. That might very well be the case. Obviously the ISHLT criteria were created for double LTC. It is difficult to tease that out. That is certainly a possibility.

Dr Keshavjee. Thank you very much.

Dr David M. Follette *(Sacramento, Calif)*. I have 2 questions. As we moved toward more aggressive use of marginal donors, donor management strategies changed and improved. Were there any changes in donor management strategies in your OPO that might have contributed to having better lungs going in? You mentioned one that we had talked about many years ago, which was the use of steroids, but there are other factors that might have contributed.

Dr Ailawadi. That is also a little bit difficult to tease out. Overall, I would say that we seem to be using a lot more marginal donors now than we have in the past. Our center has matured and has had experience with more marginal donors. I probably cannot say that there is anything that we can pinpoint that is different aside from OPO changes that have happened across the board at all institutions.

Dr Follette. We found in San Francisco that as we got better at taking care of marginal donors, we took even better care of the ideal donors.

The second question is the opposite approach of the last question our primary discussant asked. You used significantly more double LTXs in your second cohort, and perhaps some of us felt from Dr Patterson's teachings many years ago that double LTXs, well taken care of, might actually make the duration of your damage shorter. Do you think part of your excellent result is because you had a statistically significant increase in the number of double LTXs versus single LTXs?

Dr Ailawadi. It could be possible, although during the current era of the study period, only 25% of our LTXs were double LTXs, and therefore I am not sure whether I can draw that conclusion. This has currently changed at our institution within the last 3 years. More than 60% of our LTXs currently are double LTXs based on data from the ISHLT reports over the last several years, suggesting that there is a benefit.

Dr K. Robert Shen *(Rochester, Minn)*. Last year at this meeting, you had reported on less acute rejection, less bronchiolitis obliterans syndrome, and improved overall survival at your center after a change in the induction regimen from an ATG-based regimen to daclizumab. In your data were you able to assess the effect of the changes in the induction regimen in the 2 study periods? Do you have any comment on that?

Dr Ailawadi. The outcomes that we studied in that report were not 30-day mortality. They were long-term mortality, acute rejection, and bronchiolitis obliterans syndrome. We did not link those data with the 30-day data and PGD with this study. Furthermore, ATGAM is not given to patients with evidence of RI or PGD. I do not think the induction agent played an important role in RI.